Scientific Abstract

In this study, we will apply the technique of direct gene transfer to enhance immune response against cancer tumors *in vivo*. The intent of this proposed immunotherapy for cancer is to evaluate the clinical response to the expansion of lymphocytes which respond specifically to tumor antigens.

Patients with advanced cancer who have failed conventional therapy, will undergo a procedure in which a plasmid DNA/lipid complex will be injected directly into the tumor mass. The plasmid DNA encodes the human cytokine, Interleukin-2 (IL-2), in a non-viral plasmid eukaryotic expression vector.

Recombinant IL-2 protein has been approved for cancer immunotherapy in renal cell carcinoma, and is undergoing advanced clinical evaluation for malignant melanoma. The proposed study enables production of IL-2 directly in the tumor in order to recruit immune cells to the tumor site, cause immunologic recognition of specific tumor antigens, and thus cause subsequent tumor regression.

Increasing doses of the DNA/lipid complex will be administered to patients with a variety of solid tumors or lymphomas. If no toxicities are observed, the procedure will be repeated up to six times. The specific objectives of this study are to: 1) determine safety and toxicity associated with doses of this DNA /lipid complex; 2) confirm *in vivo* expression of IL-2 in tumor cells; 3) determine biological activity and pharmacokinetics of the treatment; and 4) determine whether expression of IL-2 gene product stimulates tumor regression, in patients with metastatic malignancies (either solid tumors or lymphomas). This immunotherapy may provide a potent therapeutic effect in cancer, based on a novel therapy using a well-characterized cytokine in a potentially toxicity-free delivery mechanism.